DOI: 10.1111/jdv.16849 JEADV

POSITION STATEMENT

The evolving field of Dermato-oncology and the role of dermatologists: Position Paper of the EADO, EADV and Task Forces, EDF, IDS, EBDV–UEMS and EORTC Cutaneous Lymphoma Task Force

C. Garbe,[1,*] K. Peris,[2,3] E. Soura,[4] A.M. Forsea,[5] A. Hauschild,[6] M. Arenbergerova,[7] M. Bylaite,[8] V. del Marmol,[9] V. Bataille,[10,11] M. Samimi,[12] S. Gandini,[13] P. Saiag,[14] T.K. Eigentler,[15] A. Lallas,[16] I. Zalaudek,[17] C. Lebbe,[18] J.-J. Grob,[19] C. Hoeller,[20] C. Robert,[21,22] B. Dréno,[23] P. Arenberger,[7] L. Kandolf-Sekulovic,[24] R. Kaufmann,[25] J. Malvehy,[26,27] S. Puig,[26,27] U. Leiter,[1] S. Ribero,[28] E. Papadavid,[29] P. Quaglino,[28] M. Bagot,[18] S.M. John,[30] M.-A. Richard,[19] M. Trakatelli,[31] C. Salavastru,[32] L. Borradori,[33] B. Marinovic,[34] A. Enk,[35] C. Pincelli,[36] D. Ioannides,[16] C. Paul,[37] A.J. Stratigos[4]

[1]Center for Dermato-oncology, Department of Dermatology, Eberhard Karls University of Tuebingen, Tuebingen, Germany
[2]Dermatologia, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy
[3]Dermatologia, Università Cattolica del Sacro Cuore, Rome, Italy
[4]1st Department of Dermatology-Venereology, Andreas Sygros Hospital, National and Kapodestrian University of Athens, Athens, Greece
[5]Department of Oncologic Dermatology, University Hospital Elias, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania
[6]Department of Dermatology, University of Kiel, Kiel, Germany
[7]Department of Dermatovenereology, Third Faculty of Medicine, Charles University, University Hospital of Kralovske Vinohrady, Prague, Czech Republic
[8]Faculty of Medicine, Centre of Dermatovenereology, Clinic of Infectious Diseases and Dermatovenereology, Vilnius University, Vilnius, Lithuania
[9]Dermatology Department, Erasme Hospital, Université Libre de Bruxelles, Brussels, Belgium
[10]Dermatology Department, West Herts NHS Trust, London, UK
[11]Twin Research and Genetic Epidemiology Department, Kings College London, London, UK
[12]Departments of Dermatology, University Hospital of Tours, Tours, France
[13]Molecular and Pharmaco-Epidemiology Unit, Department of Experimental Oncology, IEO, European Institute of Oncology IRCCS, Milan, Italy
[14]Department of General and Oncologic Dermatology, Ambroise-Paré Hospital, APHP, & EA 4340, 'Biomarkers in Cancerology and Hemato-Oncology', UVSQ, Université Paris-Saclay, Boulogne-Billancourt, France
[15]Departments of Dermatology, University Hospital Tübingen, Tubingen, Germany
[16]First Dermatology Department, Medical School, Aristotle University of Thessaloniki, Thessaloniki, Greece
[17]Department of Dermatology, University of Trieste, Trieste, Italy
[18]Department of Dermatology, AP-HP Saint Louis Hospital, Paris, France
[19]Timone Hospital, Aix-Marseille University, Marseille, France
[20]Department of Dermatology, Medical University of Vienna, Vienna, Austria
[21]Department of Cancer Medicine, Gustave Roussy Cancer Campus, Villejuif, France
[22]Paris-Saclay University, Le Kremlin Bicêtre, France
[23]Department of Dermatolo-Cancerology, CHU Nantes, CIC 1413, CRCINA, University Nantes, Nantes, France
[24]Department of Dermatology, Faculty of Medicine, Military Medical Academy, University of Defense, Belgrade, Serbia
[25]Department of Dermatology, Venerology and Allergology, University Hospital Frankfurt, Frankfurt am Main, Germany
[26]Dermatology Department, Hospital Clinic of Barcelona, University of Barcelona, Spain
[27]Institut d'Investigacions Biomédiques August Pi i Sunyer (IDIBAPS), Biomedical Research Networking Centre on rarae disease (CIBERER), ISCIII, Barcelona, Spain
[28]Dermatology Clinic, Department of Medical Sciences, University of Turin, Turin, Italy
[29]2nd Department of Dermatology-Venereology, ATTIKON Hospital, National and Kapodistrian Univeristy of Athens, Athens, Greece
[30]Department Dermatology, Environmental Medicine, Health Theory, University of Osnabrueck, Osnabrueck, Germany
[31]2nd Department of Dermatology-Venerology, Papageorgiou Hospital, Aristotle University of Thessaloniki, Thessaloniki, Greece

EADO, European Association of Dermato-Oncology; EADV, European Academy of Dermatology and Venereology (EADV Tasks Forces on Melanoma and NMSC); EDF, European Dermatology Forum; IDS, International Dermoscopy Society; EBDV–UEMS, European Board of Dermatovenereology of the European Union of Medical Specialists

[32]Pediatric Dermatology Discipline, Dermato-oncology Research Facility, Colentina Clinical Hospital, Bucharest, Romania
[33]Department of Dermatology, University Hospital of Bern, Inselspital, Bern, Switzerland
[34]Department of Dermatology and Venereology, University Hospital Center Zagreb, School of Medicine University of Zagreb, Zagreb, Croatia
[35]Department of Dermatology, University Hospital of Heidelberg, Heidelberg, Germany
[36]DermoLab, Dermatology, University of Modena and Reggio Emilia, Modena, Italy
[37]Department of Dermatology, Toulouse University, Toulouse, France
*Correspondence: C. Garbe. E-mail: claus.garbe@med.uni-tuebingen.de

Abstract

Background The incidence of skin cancers has been increasing steadily over the last decades. Although there have been significant breakthroughs in the management of skin cancers with the introduction of novel diagnostic tools and innovative therapies, skin cancer mortality, morbidity and costs heavily burden the society.

Objective Members of the European Association of Dermato-Oncology, European Academy of Dermatology and Venereology, International Dermoscopy Society, European Dermatology Forum, European Board of Dermatovenereology of the European Union of Medical Specialists and EORTC Cutaneous Lymphoma Task Force have joined this effort to emphasize the fundamental role that the specialist in Dermatology–Venereology has in the diagnosis and management of different types of skin cancer. We review the role of dermatologists in the prevention, diagnosis, treatment and follow-up of patients with melanoma, non-melanoma skin cancers and cutaneous lymphomas, and discuss approaches to optimize their involvement in effectively addressing the current needs and priorities of dermato-oncology.

Discussion Dermatologists play a crucial role in virtually all aspects of skin cancer management including the implementation of primary and secondary prevention, the formation of standardized pathways of care for patients, the establishment of specialized skin cancer treatment centres, the coordination of an efficient multidisciplinary team and the setting up of specific follow-up plans for patients.

Conclusion Skin cancers represent an important health issue for modern societies. The role of dermatologists is central to improving patient care and outcomes. In view of the emerging diagnostic methods and treatments for early and advanced skin cancer, and considering the increasingly diverse skills, knowledge and expertise needed for managing this heterogeneous group of diseases, dermato-oncology should be considered as a specific subspecialty of Dermatology–Venereology.

Received: 1 July 2020; Accepted: 13 July 2020

Conflict of interest

Claus Garbe reports personal fees from Amgen, grants and personal fees from NeraCare, grants and personal fees from Novartis, personal fees from Philogen, grants and personal fees from Roche, grants and personal fees from Sanofi, personal fees from BMS, personal fees from MSD, outside the submitted work; Ketty Peris reports personal fees for Advisory Board Meeting from Almirall, and AbbVie from, Biogen, Lilly, Celgene, Galderma, Leo Pharma, Novartis, Pierre Fabre, Sanofi, Sandoz, Sun Pharma and Janssen outside the submitted work. Ana Maria Forsea reports Congress participation sponsoring and fees for scientific consultancy from Merck, Leo Pharma, Solartium, Novartis, without conflict of interest and without relationship to the current work. Axel Hauschild reports personal fees and/or research support from Amgen, BMS, Merck Serono, MSD/Merck, Philogen, Pierre Fabre, Provectus, Regeneron, Roche, OncoSec, Almirall Hermal, Sanofi-Genzyme, Sun Pharma and Novartis Pharma outside the submitted work. Monika Arenbergova reports personal fees as a speaker/consultant from MSD and BMS. Matilda Bylaite-Bucinskiene reports personal fees from Roche, Eucerin, AbbVie and Sanofi. Mahtab Samimi received fees for an educational programme from BMS. Philippe Saiag has received personal fees from Amgen, Bristol-Myers Squibb, MSD, Merck Serono, Pfizer, Roche-Genentech, Pierre Fabre and Novartis outside the submitted work, and has received non-financial support from Bristol-Myers Squibb, MSD, Roche-Genentech and Novartis. Thomas Eigentler reports personal fees for Advisory Board Meetings from Novartis, Roche, BMS, MSD, Leo Pharma, Sanofi and Pierre Fabre outside the submitted work. Iris Zalaudek reports personal fees for Advisory Board Meetings from Novartis, Pierre Fabre, Sanofi, Sun Pharma and La Roche Posay. Jean Jacques Grob reports honoraria as an Advisor for BMS, MSD, Novartis, Amgen, Pierre Fabre, Roche, Pfizer and Merck Darmstadt. Brigitte Dréno reports personal fees for Advisory Board Meetings from Almirall, Galderma, Leo Pharma, Pierre Fabre, Sanofi, Sun Pharma, BMS and Roche. Lidija Kandolf Sekulovic reports personal fees and non-financial support from MSD, and personal fees from Novartis, Roche, BMS and AbbVie. Josep Malvehy reports personal fees and/or research

support from Novartis, Roche, BMS, Pierre Fabre, Sun Pharma, AbbVie, Sanofi, Regeneron, Almirall, ISDIN, Amgen, Cantabria, Melagenix, Castle Biosciences, AMLo Biosciences and Pfizer outside the submitted work. Ulrike Leiter reports honoraria and personal fees for advisory board meetings from Roche, Novartis, Sun Pharma, MSD and Pierre Fabre. Veronique Bataille reports fees for talks and teaching from BMS and Novartis. Pietro Quaglino reports advisory board fees from Takeda, Kiowa-Kirin, Therakos, Innate Pharma, Helsinn-Recordati, BMS, Novartis, Merck-Pfizer, MSD, Sun Pharma, Pierre Fabre and Sanofi. Myrto Trakatelli reports personal fees and/or research support from Novartis, Leo Pharma, Genesis Pharma, Sanofi and UCB, and no conflicts of interest related to the subject. Dimitrios Loannides reports personal fees and/or research support from AbbVie and Janssen. Alexander J. Stratigos reports personal fees and/or research support from Novartis, Roche, BMS, AbbVie, Sanofi, Regeneron and Genesis Pharma outside the submitted work.

Funding source

There was no funding for this paper.

Introduction

Dermato-oncology is a rapidly evolving branch of Dermatology–Venereology focusing on the prevention and management of both common and rare forms of cutaneous malignant tumours, ranging from melanoma and epithelial skin cancers to tumours of neuroendocrine and lymphoid origin. The strong increase in the incidence of melanoma and other skin cancers, enhanced by increased life expectancy and population ageing along with the introduction of *in vivo* diagnostic tools (e.g. dermatoscopy) and new treatments for advanced melanoma and non-melanoma skin cancers (NMSCs) have resulted in unprecedented changes in the organization of patient care in the clinical setting. The present paper highlights current priorities in the field of dermato-oncology (as illustrated in Fig. 1) and reviews the fundamental role of dermatologists in the prevention, diagnosis and treatment of skin cancer.

Mastering the skin cancer epidemic

The incidence of skin cancers is increasing across all Europe, although with different speed and patterns across East-West and North-South regions (Fig. 2).[1,2] With few limited exceptions,[3] this trend is expected to continue strongly. In Central Europe, the incidence of melanoma and NMSCs was roughly 1 and 5 cases per 100 000 in 1950, respectively.[4,5] In Germany, 25 and 250 cases per 100 000 inhabitants have been diagnosed with melanoma and NMSC in 2010, respectively, and about 45 and 400 cases of melanoma and NMSCs per 100 000 inhabitants, respectively, are expected in 2030.[6,7] It is estimated that, over a period of 80 years, the incidence of melanoma will increase 45-fold and that of NMSC 80-fold. There are similar increases in the incidence of skin cancer in Western white populations worldwide.[3] So far, in Europe there is no clear trend of reversal, while in Australia the first signs of a levelling-off of the incidence of melanoma have been observed, eventually driven by significantly higher numbers of patients with skin cancers.[3]

In order to better understand the skin cancer epidemic, it is important to recognize its two driving forces: the massive increase of human exposure to ultraviolet radiation (UVR) in the last half-century, and the ageing of the population – especially the skin cancer-prone Caucasian population (Table 1). It has been well established epidemiologically that melanoma, as well as most NMSCs, is mainly caused by UVR.[8,9] In Australia and the United States, about 95% of cutaneous melanomas are estimated to be caused by UVR.[10,11] Several other factors play a role in the increasing trends of skin cancer, such as the increase in early diagnosis and reporting of cases through increased awareness, improved diagnosis, as well as expanding cancer registries. In contrast with the dramatic increase in incidence, the mortality of skin cancers is plateauing,[1,12] a trend which is usually attributed to improved management, but also raises the question of overdiagnosis as a result of increased diagnostic scrutiny. There is also a staggering increase in the medical costs of diagnosis and management, with the use of more complex diagnostic testing and expensive innovative drugs for advanced disease, now also employed in earlier stages of the disease as adjuvant treatment. In a recent study from Australia, it was reported that the mean annual cost per patient for melanoma stage 0/I/II was US$1175, rising to US$80 440 for stage III/IV.[13] In addition, the treatment of basal cell carcinoma and squamous cell carcinoma in 2011 in the United States was associated with costs of up to US$4.8 billion.[14] Thus, the increased incidence causes a 'snowball' of growing mortality and morbidity burden, as well as of human, societal and material costs, which are all facets of the complex 'skin cancer epidemic'.

In order to address this epidemic, action needs to be taken at multiple levels: (a) primary prevention – actions towards reduction of UVR exposure in the general and high-risk populations, (b) secondary prevention, mainly focusing on the early detection of thick, aggressive tumours and tumours that develop in individuals at high risk for unfavourable outcomes, and (c) expansion and improvement of skin cancer registration in order to

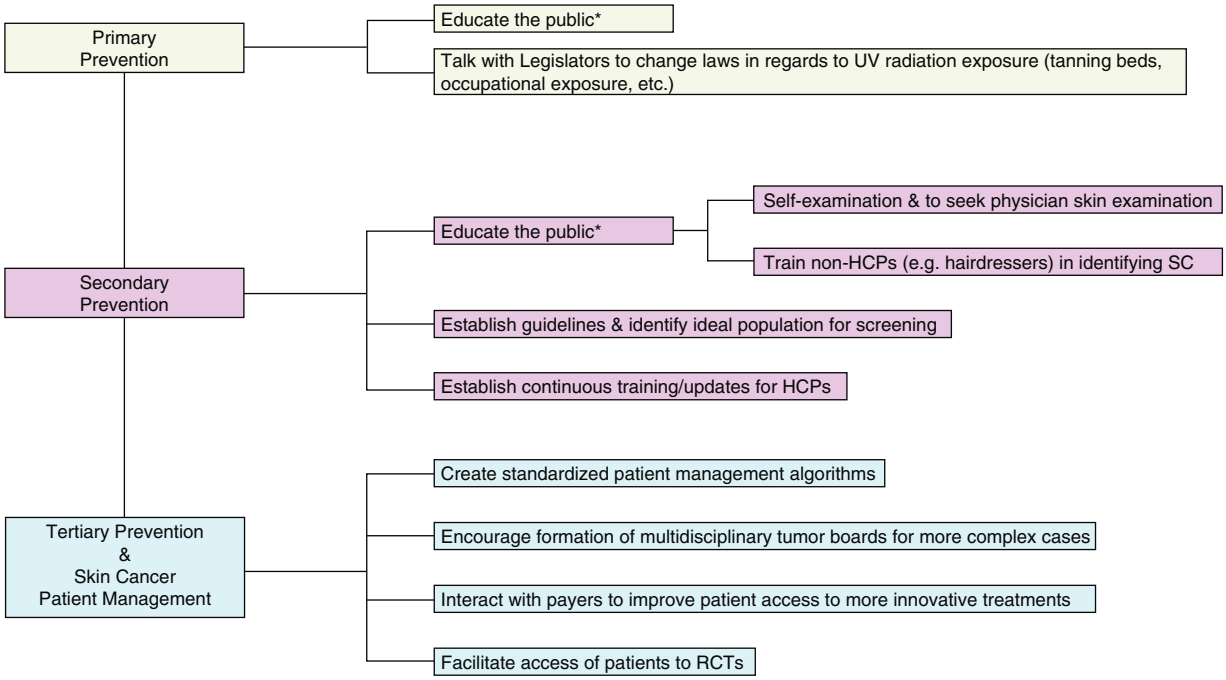

Figure 1 Actions/priorities in dermato-oncology. *Collaborate with authorities and scientific communities to organize campaigns and other actions. HCPs: healthcare providers; RCTs: randomized controlled trials; SC: skin cancer; UV: ultraviolet.

generate data that will allow specialists to monitor the epidemic, measure the efficacy of preventive strategies and plan appropriate interventions.

For improvement of cancer reporting, pressure by the civil society, including not only researchers and physicians, but also the patients and public, should be put on policymakers and stakeholders to 'listen to science'[15] and allocate the appropriate resources and priorities to the building and maintenance of high-quality, independent-functioning and open-research, population-based cancer registries across all European regions. Without them, any efforts to master the cancer epidemic would be like a journey without a compass.

Reorientation of primary and secondary prevention

Despite numerous preventive initiatives and increased public awareness, the burden of skin cancer on public health remains significantly high. Therefore, there is an urgent need to critically review the existing skin cancer prevention strategies, in order to determine where targeted efforts may improve patient outcomes.[16–18]

Primary skin cancer prevention is mainly focused on limiting the amount of solar UV exposure and avoiding artificial UVR exposure (i.e. sunbeds). Although skin cancer can affect any individual at any age, it usually develops in individuals over 50. The modifiable risk factors for skin cancer relate to UVR exposure behaviours, such as a history of prolonged sun exposure (either at work or for leisure), a history of sunburns, especially in younger ages, and regular use of sunbeds. These add to genetic and phenotypical factors like having more than 50 moles on the whole body, having fair skin or propensity to sunburn, a family history of melanoma/skin cancer or immunosuppression (e.g. organ transplant recipients [OTRs]). Avoiding excessive UV exposure, especially in childhood and adolescence, is thus a cornerstone in any public health prevention initiative.[19–22]

Sunscreens have been an important component to this strategy and, as shown in prospective controlled studies, their regular use has a protective role against melanoma and certain types of skin cancer (e.g. NMSCs).[23] However, their use as an effective protective agent against UVR remains more of a feasibility issue in terms of the frequency and amount of sunscreen needed for optimal protection. Due to unclear messages, the general population seems to erroneously believe that the exclusive use of sunscreens during sunbathing eliminates or significantly reduces the effect of sunbathing on melanoma and NMSC risk. On the other hand, it is important to consider that UVR also has several

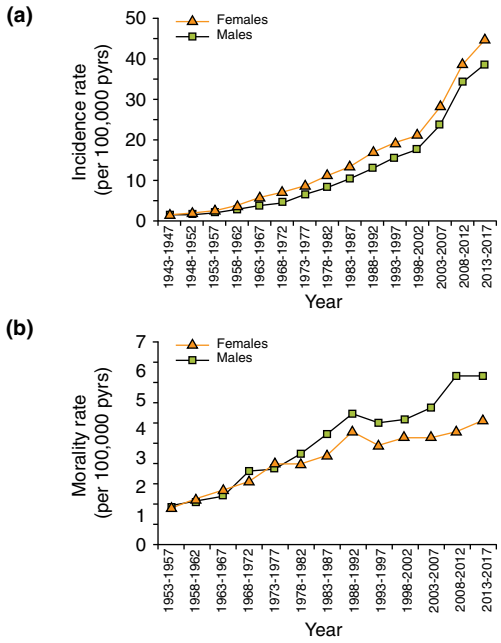

Figure 2 Data regarding cutaneous melanoma in Germany. The Danish Cancer Registry records the incidence of melanoma since 1943 and mortality since 1953, and has the longest continuous documentation in Europe. The crude incidence and mortality rates are presented here, which also reflect demographic changes with increased life expectancy in contrast to age-standardized rates. (a) Crude incidence rates for males and females 1943 - 2017 (b) Crude mortality rates for males and females 1953 – 2017. (Graph developed from the freely accessible data from the Danish Cancer Registry: https://www-dep.iarc.fr/NORDCAN/english/frame.asp).

Table 1 Causes of increased UVR exposure of populations

- Massive increase in intentional exposure after the Second World War, motivated by the desire to get a tan with sunbathing and tanning salons, in contrast to sun avoiding behaviour before this period (a tan has become desirable, heavily promoted as the new beauty and attractiveness ideal).
- Unintentional exposure and incidental sunburns resulting from the radical change of lifestyle (holidays, global travel, outdoor sports) and fashion style.
- Occupational exposure (i.e. unprotected exposure of outdoor workers).

positive effects for our overall health by enhancing our mood, relieving stress, improving sleep, treating seasonal depression and maintaining vitamin D production. Although strict sun avoidance is not required, skin cancer primary prevention measures that include sun protection should be implemented. Our main message should emphasize that being sun-safe is compatible with all hobbies, sports or activities (except tanning for tanning's sake), and that protection from excessive sun exposure should be done through a common-sense combination of methods, including shade, clothing, sunglasses and broad-spectrum

Table 2 Summary of sun protection measures

- **Avoid intentional UV exposure** with the purpose of getting a suntan (both natural sunbathing and sunbeds).
- **Avoid or limit sudden, unintentional, intense direct exposure to the sun while working or pursuing leisure activities.**
- **Encourage UV protection through clothing.** Clothing provides the best protection from intense sunlight: a wide-brimmed hat, UV ray-filtering sunglasses (since UV rays are also harmful to the eyes) and T-shirts (preferably darker-coloured clothing of tightly woven material, and for intense insolation with certified UV protection). Clothing and swimming suits for children with built-in sun protection [up to sun protection factor (SPF) 50] are available.
- **Provide shade** – encourage institutions to provide shading structures as far as possible in schools, play areas, sports facilities or outdoor working sites.
- **Employ supplementary use of sunscreens in areas of the body that cannot be protected by clothing.** Sunscreen should have the highest SPF and provide equal protection from UVA and UVB rays. Sunscreen products are effective immediately after they are applied to the skin. However, the dose normally used is much lower than necessary to achieve the stated SPF. It is therefore recommended to apply them once in the morning and a second time immediately before sun exposure. They should be reapplied after bathing or heavy sweating.

high SPF sunscreens for uncovered body parts [24,25]. Along this line, sunscreens need to be positioned as auxiliary methods of protecting uncovered, limited body surfaces, for a limited time, not replacing shade and clothing and not extending the time in the sun. The use of sunscreen as part of a daily routine to reduce incidental sun exposure will also contribute to reducing overall UVR-induced skin damage (Table 2).

Secondary prevention encompasses the various strategies of early detection of skin tumours, including skin cancer screening (SCS) programmes. These strategies are expected to reduce the epidemiologic burden and the cost of skin cancer management, on the premise that skin cancer can be more easily and effectively treated at an early phase of development. In 2008, a nationwide SCS programme for the general population was introduced in Germany. So far, it is credited with contributing to earlier detection and treatment of skin cancer,[26] but it has not clearly proven to reduce melanoma mortality. With insufficient scientific evidence supporting its benefits, the applicability for general population SCS is limited. Therefore, shifting and better targeting screening efforts towards high-risk groups, including men over 60 years of age, immunosuppressed patients like OTRs or patients with HIV/AIDS, and socioeconomically less-privileged individual,[27–29] could prove to be a more effective approach in improving the outcomes of secondary prevention measures.[12,30] Additional high-risk groups, such as patients on immune-mediated treatments for chronic inflammatory conditions and cancer survivors, should also be a focus of targeted prevention.

Dermatologists are the best trained and equipped specialists to provide early detection, but their success depends on insuring the timely access of patients to their services. There are several

studies showing that detection of earlier stage melanoma and improved patient survival is associated with care by a dermatologist rather than a non-dermatologist.[31] In addition, a greater density of dermatologists in a given geographical area has been associated with lower melanoma mortality compared to areas lacking dermatologists.[31] These results suggest that increasing access to dermatologists may represent a useful approach to improving melanoma-related health outcomes.[32] Still, dermatologists cannot realistically see the whole population at random twice a year. This fact points to the major role of self-surveillance and self-examination together with raising public awareness. New digital technologies, including smartphone apps, can be used for health education and to support skin self-examination and lesion monitoring, complementing access to the expert dermatologist. In a personalized medicine era, individual patients are willing to participate in more aspects of their health care. Although primary and secondary prevention are beneficial and cost-effective,[14,33–35] it is important to optimize ways to improve the dissemination and effectiveness of all types of prevention measures.

Quality assurance in the diagnosis and treatment of skin cancer – Guideline development

Quality assurance relies on the implementation of highly standardized procedures in diagnosing, documenting and treating cutaneous tumours. 'Standard operating procedures' (SOPs) must be designed based on high-quality evidence-based medicine data and ideally should be implemented in all cancer centres. Quality assurance generally consists of three steps: (a) assessment of the quality of current procedures and identification of gaps and problems with care delivery, (b) designation of interventions to improve and solve them, and (c) prospective assessment of the implementation of designed interventions to make sure that the tasks have been well carried out. Quality assurance relates to all diagnostic and therapeutic procedures across the whole continuum of management, namely rapid and easy access to early diagnosis using appropriate diagnostic methods (i.e. dermatoscopy, digital dermatoscopy), standardized biopsy procedures, standardized complete histopathology reports, appropriate risk classification and staging, appropriate surgery and medical management and follow-up according to clinical practice guidelines.

An example of implementing SOPs in daily care of patients with skin cancer is the accurate documentation of cutaneous tumours and informed selection on the methods of diagnosis and treatment. If a skin cancer is suspected, clinical characteristics such as the lesion's location and diameter should be recorded and macroscopic and dermatoscopic photographic images should be captured and stored in the patient's medical file. All these data should be available prior to surgery in order to optimize the histopathological evaluation and quality of diagnosis. The standard therapy for skin cancer is surgical excision followed by histopathological examination.[36,37] A partial biopsy (incisional, punch or shave) can be an alternative option to the standard excisional biopsy in large tumours, tumours located on sensitive areas (e.g. face and genitalia), and recurrent or difficult-to treat tumours, in order to confirm the diagnosis and plan a subsequent complete excision or medical treatment. Destructive (blind) procedures such as curettage, cryotherapy and laser ablation, as well as non-surgical treatments including photodynamic therapy and topical therapies, either alone or combined, do not allow for histopathological diagnosis and assessment of the entire tumour.[36,37]

There is evidence that the quality of care for skin cancer, particularly for NMSC, differs between primary care and dermatology. In a systematic review done in the UK, excisions led by dermatologists had the highest overall and disease-free survival rates compared to general practitioners (GPs), whereas plastic surgeons were most likely to excise complex lesions on difficult-to-treat areas.[38] In a large cross-sectional study in the Netherlands, BCCs were more often completely excised by dermatologists than by GPs and plastic surgeons due to the dermatologist's extensive training and high experience in BCC care.[39] These findings support the need for education and collaboration with other specialties, as discussed hereafter.

A significant challenge to ensuring quality care for all skin cancer patients is the high disparities across the whole continuum of cancer care, manifest in Europe along a North-South, West-East gradient. Eastern European countries have reported poorer outcomes of skin cancer,[40,41] face more frequent late diagnosis,[42,43] have less capacity for skin cancer registration and reporting,[44] lag behind in preventive efforts,[45] are less well equipped for early diagnosis[46] and struggle with important shortcomings in access to innovative life-saving therapies for skin cancers.[47] Therefore, the European guidelines, recommendation of best practice, certification and other initiatives of quality assurance must be accompanied by a constant preoccupation of supporting and monitoring their implementation in countries facing challenges, so that the minimal requirements for quality cancer care in skin cancer [48] are met across the entire continent, without painful gaps.

Professional Societies and National Medical Societies produce and frequently update guidelines in order to introduce evidence- or expert-based recommendations for high-quality, standardized care. Over the last decade, the EDF, EADO and EORTC have been very successful in developing European guidelines covering all major skin cancers. The first European guideline on melanoma appeared in 2010 and was updated in 2013, 2016 and 2019.[37,49] In 2019, guidelines for basal cell carcinoma were published and those for squamous cell carcinoma were updated.[36,50] Furthermore, European guidelines for dermatofibrosarcoma protuberans, Merkel cell carcinoma and Kaposi's sarcoma were reported.[51–53] These guidelines, which are led by dermatologists, are continuously updated in cooperation with the above-mentioned European medical societies.

Establishment of multidisciplinary skin tumour centres

Treating patients with cancer in dedicated wards began at the end of the 18th century in the United States and mid-19th century in Europe, but the formalization and accreditation of comprehensive cancer centres at the national and even European level emerged only recently, in the early 2000s.[54,55] At present, high-quality cancer care should be patient-centred and for skin cancers, such care requires clear pathways with reasonable and traceable timelines, in either direction, between GPs, dermatologists and multidisciplinary skin tumour centres (MSTCs). The patients' journey should be adapted to the patients' needs which may vary from one country or region to another. A MSTC has five major interconnected missions: (a) clinical management of patients, (b) research, (c) education and training, (d) quality assurance capacities and (e) participation in national and European networks. Providing high quality of care relies on decisions taken within multidisciplinary tumour boards by a multidisciplinary team (MDT) where dermatologists/dermato-oncologists are key players in the management of skin cancers.

A MDT meets at least every week, discusses the most complex cases and decides the best possible management or treatment for each individual patient. The assurance of quality of care is closely related to qualification and experience of each member of the group. Therefore, the core of the MDT is represented by board certified dermatologists with a special interest or certification in oncology (dermato-oncologists) with good experience in the diagnosis and management of skin cancer including the use of targeted therapies, immunotherapies and chemotherapies, or medical oncologists with a specific and dedicated interest in skin cancers. Around this core group, MDT includes other professionals with good knowledge and experience on skin cancers: surgeons (dermatosurgeons, plastic surgeons, surgical oncologists), pathologists, molecular pathologists, radiologist(s), including interventional radiologists, nuclear medicine physicians and radiotherapists. The expertise of various other disciplines is frequently needed: geriatric oncologists for patients over 75 years old, pharmacists, psycho-oncologists, palliative care, specialized/advanced practice nurses and study coordinators.

Multidisciplinary skin tumour centre gain expertise from management of a sufficient number of patients per year, and some countries have proposed thresholds (e.g. 20 advanced melanomas per year in the Netherlands, 40 in Germany).[48] This is even more important for rare skin cancers, such as Merkel cell carcinoma, sarcomas and adnexal tumours, which should be managed in the context of dedicated networks. Decisions for MSTCs should be based on European and/or national guidelines published in peer-reviewed scientific journals, shared with the team and proposed transparently to patients who need to be involved in the decisions. In addition, access to innovative therapies through clinical trials should be available either in the centre or by referring patients to other centres. Contribution from MSTCs to national and European registries and biobanks should be also encouraged. Clinical, process and patient-reported outcomes, including severe adverse events, overall survival rates and adherence to guidelines, should be measured, regularly audited (internal and external audits) and made available to patients. Finally, education programmes for professionals and patients should be offered not only at MSTCs but also in the context of regional, national and international networks.[48,56]

Development of integrative dermato-oncology

The complexity of skin cancer care is exploding, with rapidly evolving new options in adjuvant, loco-regional and systemic treatment, along with a changing paradigm for surgical approaches. This is paralleled not only by new concepts of molecular classification and prognostic markers, an increasing demand to manage challenging new adverse effects, but also a set of new survivorship issues in the context of unprecedented survival rates through innovative therapies. In this setting, the optimal skin cancer care is the patient-centred one. As discussed above, this implies a multidisciplinary discussion and decision on each individual case, but at the same time also requires an integrated implementation of the decided care plan.[48]

This integration needs to be achieved at multiple levels: joint care under the supervision of one case-managing specialist, integrated care in terms of facilities and infrastructure used, and an integrated reimbursement plan for the whole care continuum.

The bundling of diagnosis, surgical therapy and systemic therapy in one team is preferred by patients, increases the competence for an individualized therapy and can facilitate treatment adherence. There are currently three models of care of dermato-oncology in Europe: (a) integrated care under the charge of dermatology specialists with dermato-oncological competence (German-speaking countries, France, some centres in Czech Republic, Serbia and other countries), (b) diagnosis and surgery together, with systemic therapy by oncologists and/or dermatologists (Mediterranean countries), and (c) diagnosis by dermatologists, surgery by surgeons/plastic surgeons with systemic therapy by medical oncologists (United Kingdom, Scandinavia and the majority of Eastern Europe).[54]

The last model increasingly occurs under pressure in the current complex healthcare context. It often leads to fragmented care, with lack of communication and information sharing between specialties, use of different specialty-specific sets of national guidelines and therapy protocols, lack of comparability and agreement on results of diagnostic tests, and foremost the need for typically fragile patients to be physically moved between offices, wards, hospitals, and even cities, as not all necessary facilities and administrative checkpoints are in one place. The development of adjuvant and neoadjuvant therapy also interferes with the efficacy of this model. The different recommendations

received within a few weeks by multiple specialists may be confusing for the patient.

Integrative dermato-oncology is well supported by the current successful model of German-speaking countries and France.[57] It is further corroborated by the fact that dermatologists are the most informed about the natural course and particularities of skin tumours, they are already experienced in the diagnosis, local surgical or non-surgical treatment, and follow-up of skin tumours, as well as the management of skin toxicities of oncological therapies. Thus, dermatologists are already an indispensable part of the skin cancer patients' management along all steps of their care continuum. Moreover, due to their current curricula and training as reflected in the standard of the Union Européenne des Médecins Spécialistes (UEMS), dermatologists have solid internal medicine training, are trained to manage autoimmune diseases and severe reactions, and currently manage systemic immune-biological drugs (like in psoriasis, atopic dermatitis, autoimmune diseases). In addition, the EADO has set up a programme to help train specialists in dermato-oncology. This includes the annual conference of the European School of Dermato-Oncology in Berlin, a fellowship programme with internships in interdisciplinary skin tumour centres and both examinations and certificates in systemic therapy of tumours.

Whenever possible, the dermatologist with competence in dermato-oncology should be in charge of the integrated care of skin cancer patients on the whole continuum, not only prevention and diagnosis but also systemic treatment, including clinical trials and follow-up, under consultation with the multidisciplinary tumour board and in close cooperation with other relevant specialties. The legislative, administrative and reimbursement framework should be adjusted accordingly. This should not be interpreted as competition with other specialties but as collaboration and an extension of high-quality services offered to patients to ensure integrated care and avoid the obstacles of shortages of personnel and capacity. This format of care can lead to better patient outcomes, since a higher number of qualified medical professionals are involved in patient care. For example, in countries where both dermato-oncologists and medical oncologists are prescribing systemic therapy, the mortality to incidence ratio as a surrogate marker for fatality rate is lower. Conversely, in countries where legislative restrictions to prescribe systemic therapy and reimbursement restrictions based on medical specialty exist, the mortality to incidence ratio is higher.[54]

For the development of integrative dermato-oncology, the necessary steps are as follows:

1 *Improve and optimize education and training:* It is necessary to establish standardized advanced dermato-oncology training as a supra-specialization in medical tumour therapy of skin cancers as a choice for dermatologists. Models of 1-year supra-specialization exist in Germany, Austria, France, Switzerland, Serbia, Croatia and elsewhere. This model of supra-specialization (or supra-competence) merits encouragement in other countries. A major step was the introduction of the EADO-UEMS joint certification in medical tumour therapy in dermato-oncology. Further efforts are needed at the EADO-UEMS level to standardize the recommended curricula for this. It is also important to reinforce the existing basic training in the fundamentals of skin cancer (i.e. early diagnosis, prevention, follow-up and recognition of skin toxicities) and management for all general dermatologists according to the current UEMS curricula recommendation, and to ensure that these criteria of education quality are uniformly implemented across Europe.[58] Courses and e-learning modules, developed in cooperation between EADV and EADO, have been running at the European level or are currently being developed, and would be a key contribution to ensuring uniform high-quality training and supporting the appropriate training of all dermatologists.
2 *Enhance the participation of dermatologists in multidisciplinary tumour boards:* This is predicated on the fundamental concept that the optimal personalized management plan for each patient is achieved only by multidisciplinary discussion and consensus. This reinforcement should not only be through educating dermatologists, but also through supporting administrative and regulatory change in order to facilitate the creation and functioning of MDTs on a wide scale. In some countries, it would be necessary to reformulate the legislative framework to support the functioning of MDTs and the ability of appropriately competent dermatologists to manage the integrated care of skin cancer patients. Also, in some countries it would be necessary to reformulate the reimbursement regulation to allow the dermatologist to be in charge of integrated care, under consultation with the MDT (Table 3).
3 *Authorize dermatologists to participate in clinical trials with direct investigator responsibilities:* This will allow direct access to innovative drugs and better enable dermatologists to attain early practical experience with these medications, and in the management of their side-effects. Recent surveys conducted by the EADO group point to a high need for dermatologists

Table 3 Summary of steps for the successful development of integrative dermato-oncology

- Establish standardized advanced dermato-oncology training as a supra-specialization in medical tumour therapy of skin cancers as a choice for dermatologists.
- Reinforce the existing training in skin cancer (basic level) for all general dermatologists, according to the current UEMS curricula recommendations. Ensure that these quality criteria are uniformly implemented across Europe.
- Enhance the participation of dermatologists in multidisciplinary tumour boards. Reformulate the legislative framework to support the functioning of MDTs and the ability of appropriately competent dermatologists to coordinate the integrated care of skin cancer patients.

and dermato-oncologists to develop good-quality MSTCs and improve access to innovative therapies and trials in countries with low GNI per capita.[47,59]

Optimizing tumour follow-up

Dermatologists play a central role in the follow-up of patients with skin cancers, and their role definitely extends beyond skin examination (Table 4). The follow-up of skin cancer patients is of great importance as its objectives are manifold: to detect the primary tumour's recurrences or relapses as early as possible (which immediately influences the treatment decision), to detect new secondary skin cancers early[60–62] and other possibly subsequent malignancies,[63,64] to monitor and manage the side-effects of antitumoural therapies, and also to provide patients with education, counselling and support for prevention actions, both for themselves and their families. According to the recent versions of European and other international guidelines for skin cancer from EADO, EDF, EORTC and ESMO as well as the NCCN melanoma guidelines,[37,49,65,66] the frequency and extent of follow-up visits and tests depend upon the risk of relapse and risk factors for subsequent skin cancers (e.g. multiple NMSCs, immunosuppression, multiple nevi, family and personal history of melanoma, mutation status in high-penetrance melanoma genes, and history of sunburns).

In general, the following strategies are recommended:

1 Careful evaluation of reported symptoms.
2 Clinical total body skin examination, complemented by the dermatoscopic evaluation of skin lesions and digital follow-up in patients with multiple nevi/atypical mole syndrome. Dermatoscopy, which is used by the vast majority of dermatologists, improves diagnostic accuracy, avoids unnecessary excisions and allows for early diagnosis of skin cancers.[67,68]
3 Physical examination of the scar area and regional lymph nodes.
4 Blood testing and imaging tests.

Table 4 Consensus-based European international guidelines, recommendations and general goals of follow-up of patients with skin cancer

- Identify early detection of recurrent disease (local, distant) at the earliest stage.
- Recognize and treat complications of surgical interventions (e.g. pain, lymphoedema, infections and paraesthesia) and side-effects related to systemic treatment (adjuvant, neoadjuvant or locally advanced/metastatic disease therapy).
- Diagnose subsequent secondary skin cancers and possibly other related cancers.
- Provide education of the patient and his/her/their family on self-skin examination and symptoms related to disease and on personal and family risk factors.
- Offer psychosocial support and information about the disease, diagnosis, therapy and prognosis and provide the patient and first-degree relatives with education on prevention and access to consultation in case of clinical symptoms.

The first three strategies are managed by dermatologists and are mandatory for the follow-up of all patients, while blood and imaging tests have schedules and indications that differ according to tumour stage and additional risk factors. In patients with invasive melanoma, a more intensive follow-up is recommended in the first 5 years following surgery, since most recurrences occur during this time period. However, metastasis can also occur 10 years and more after a melanoma diagnosis (especially in thinner tumours), which indicates the relevance of patient education and access to medical evaluation across a lifetime. Clinicians can recommend that their patients access numerous patient education leaflets produced online by EADV on melanoma and NMSCs, as well as other skin conditions.[69] In the EADO and NCCN guidelines, radiology tests with ultrasound, CT, MRI and/or PET/CT are considered in stage IIB, IIC, III and IV to detect asymptomatic metastasis and in any case with associated symptoms.[37,65,70,71]

In patients with epithelial skin cancers, standard follow-up facilitates early detection of secondary tumours, local recurrences and metastases.[36,50,72] No impact on survival has been shown so far, but this is reasonable since no randomized studies comparing intensive and non-intensive follow-up schedules have been conducted. In addition to improving early diagnosis of secondary and/or recurring skin cancers, follow-up examinations performed by dermatologists allow them to implement the appropriate treatment, which usually is surgical. The latter seems to be beneficial for patients, since several studies highlight that surgical treatment of skin cancers by dermatologists decreases the risk of incomplete excisions and reduces the costs of such interventions.[39,73–77]

Primary cutaneous lymphoma and rare malignant skin tumours

Besides melanoma and epithelial skin cancers, rare malignant skin tumours have recently been in the spotlight due to their increasing incidence, their distinct pathogenetic and molecular mechanisms, and their improved outcomes due to new treatments. Although for some of these tumours, such as primary cutaneous lymphomas (PCL), Merkel cell carcinoma or Kaposi's sarcoma, specific guidelines do exist, for others such as adnexal tumours, there is still a need for consensus or evidence-based management.[51–53]

Primary cutaneous lymphomas encompass a heterogeneous spectrum of lymphoproliferative diseases with different clinical presentations, histological, immunological and molecular features, among which mycosis fungoides (MF) is the most frequent. The prognosis ranges from indolent such as lymphomatoid papulosis, early-stage MF, primary marginal and follicle centre B-cell lymphoma, to aggressive forms such as Sézary syndrome, advanced-stage MF, peripheral T-cell lymphomas and diffuse large B-cell lymphoma, leg type.[78] The prevalence of PCL is increasing due to better diagnostic tools;

however, overall survival has not changed in recent years.[79] Primary prevention is not possible as there are no known predisposing environmental factors for disease prevention. Nevertheless, secondary prevention is very important, leading to detection and diagnosis at an early stage, which might lead to more effective treatment or potentially improve survival. The International prospective database Proclipi[80] has shown that there is a median delay of 3 years between first symptom development and initial diagnosis. This could be attributed to lack of a singular diagnostic test and available reliable biomarkers, making early diagnosis difficult and based on clinico-pathological correlations,[81] integrated by molecular studies (clonality) and flow cytometry (for differential diagnosis of Sezary syndrome with other erythrodermic diseases as well as proper staging of patients).[82] Therefore, it is very important to address all cutaneous lymphoma suspicions to specialist reference teams to allow for proper clinico-pathological diagnosis and to define the best management. This can be done through specialized lymphoma centres with MDTs (dermatologists, haematologists, oncologists and pathologists) with appropriate diagnostic facilities such as histopathology and immunology for flow cytometry, as well as the best treatment approach at the right time like total-skin electron beam (TSEB) radiotherapy, extracorporeal photopheresis and allogeneic transplantation. New techniques are becoming available and allow a small amount of genetic material to detect malignant DNA such as T-cell receptor rearrangement with high-throughput sequencing, and next-generation sequencing (NGS) vs. Sanger sequencing. Thus, dermatologists play a major role in the diagnosis, treatment and follow-up of these patients. However, this is framed only in the context of a multidisciplinary approach where, according to the diagnosis and clinical stage, other colleagues from different specialities are mainly involved (the pathologist and molecular biologist for diagnosis, and radiotherapist, oncologist or haematologist for treatment). Indeed, treatment options range widely from skin-directed-therapies (e.g. topical steroids, phototherapy, radiotherapy either as localized or TSEB radiotherapy), systemic treatments (e.g. retinoids, low-dose methotrexate, interferons or photopheresis), immunotherapy (e.g. rituximab, brentuximab or alemtuzumab) and chemotherapy (e.g. gemcitabine, doxorubicin or CHOP) to allogeneic bone marrow transplantation.[83–85]

The combination of accurate detection of the malignant clone and mutations could lead to the development of 'personalized therapy' in a scenario of precision medicine according to patient molecular phenotype and mutations, as chemotherapy is weighted by severe side-effects and short response duration.

Innovative methods in dermato-oncology

Teledermatology

The lack of dermatologists in several European countries and population ageing along with increasing skin cancer incidence has challenged healthcare organizations. This has led to an increase in use of e-Health and teledermatology over the last 10 years. Sensitivity has been found to be comparable between teledermoscopy and face-to-face evaluations, although specificity was higher in face-to-face evaluations.[86] Many studies have shown that for SCS, up to 50% of teledermatology referrals can be downgraded to routine appointments or patients discharged with reassurance.[87–89] Up to 40% of teledermatology referrals for skin lesions are sent straight to biopsy lists without necessitating face-to-face appointments beforehand, so waiting times are reduced.[87–89] Furthermore, for large lesions, patients can be referred directly to dermatosurgeons or plastic surgeons. Most of these teledermatology clinics involve nurses taking a history and pictures, including dermoscopic images, with referrals channelled to dermatologists with a very fast turnaround.

However, since the COVID-19 pandemic, these nurse-led clinics have not been running, so dermatologists have adapted their practice. Patients have had the opportunity to use similar or adapted software where they can take photographs at home and upload them online. Video consultations are also part of several new types of teledermatology software, so if the dermatologist would like to take an in-depth history, they can speak to the patient remotely. Although dermatologists would obviously prefer to have dermoscopy pictures as this definitely improves accuracy, the use of teledermatology with photographs taken by patients and relatives for the triage of skin lesions has been invaluable during the COVID-19 pandemic. Dermatologists have been able to resolve more than 80% of teledermatology referrals and triage the patient to the appropriate pathway or advise them remotely without the need to have face-to-face visits. Inpatient referrals can also be dealt in the same way, with the ward nurses taking pictures and sending the referral online to the dermatology team. The teaching of trainees also benefits from these remote clinics, as all images and outcomes can be used for training purposes. Teledermatology software also allows for instant auditing of practices with assessment of diagnoses, turnaround times and outcomes. Therefore, there is a need to make sure that changes in practice imposed by the COVID pandemic lead to dermatology being delivered in a different way in the future, in order to avoid going back to face-to-face dermatology only for SCS whenever it is not essential.[90,91]

In recent years, a number of mobile apps in skin cancer have been launched with different categories of applications including (most commonly) teledermatology, followed by self-surveillance/diagnosis, disease guide and general dermatology. Teledermatology apps have experienced notable growth and had tripled in number from 2014 to 2017.[92]

Mobile apps and other electronic resources have the potential to improve access and outcomes for skin cancer patients, but these resources must be utilized with appropriate protocols and guidelines and with caution, as patients need to be educated about their benefits and limitations. Current algorithm-based

smartphone apps to assess images of skin tumours suspicious for skin cancer cannot be relied upon to detect malignant tumours according to the results of published studies.[93,94] Further testing must be conducted in real-life situations to evaluate the reliability of these healthcare apps for skin cancer used by patients.

Genomic medicine

Novel treatments and increasingly available and affordable NGS techniques have created an opportunity for delivering genomically informed personalized cancer therapy and prognostic estimation. Implementing the use of these technologies in the clinical setting requires a clinician's knowledge on interpreting the genetic profile of the patient, including molecular characterization of the tumour and germline DNA examination.

For the practising dermatologist and dermato-oncologist, the field of cancer genomics may appear daunting; however, the aim is not to identify all genetic alterations in the tumour or germline but instead to know how to best use emerging genetic knowledge for prognostic and therapeutic optimization. Genetics in oncology will become more important as genetic panels have been developed for many cancers and are now tested in trials including larger cohorts of patients to better predict prognosis and responses to treatment. At this stage, whole NGS of germline and somatic DNA is not used in clinical practice with the exception of very rare tumours or syndromes. However, research in the whole genomic era is moving fast with clear potentials in the areas of diagnosis, prognosis and treatment.[95]

Five to 10% of melanoma patients present with a significant family history of cancer, and this is often poorly documented. Although formal consultation by cancer geneticists is required, dermatologists should assist in the counselling and follow-up of these families. Families with multiple melanomas should undergo genetic testing using a germline familial melanoma panel (*CDKN2A*, *CDK4*, *MITF*, *BAP1*, *POT1* and other telomere genes if possible)[96] as well as tests for alterations in other cancer genes (*BRCA1*, *BRCA2*, *ATM*, etc.). It is important to establish clear indications for genetic testing in skin cancer and develop expertise in the interpretation of these panels as many variants may be, so far, classified as being of unknown clinical significance. It is clear, however, that as many more families are being tested, the significance of all reported variants will become clearer.

The identification of somatic mutations in melanoma revolutionized its treatment.[97,98] Approximately 50% of tumours harbour *BRAF* mutations, and this test is now part of standard practice in all melanoma clinics dealing with stage III and IV disease. Mutations that activate *BRAF* and *NRAS*, two critical nodes of the MAPK signalling cascade, cumulatively occur in 75% of melanomas;[99] thus, the need to test for these mutations should be known by all dermatologists and physicians involved in skin cancer treatment. The presence of *BRAF* mutations opens the therapeutic landscape to targeted gene treatments.

There are not, at this point, any specific somatic mutations that can reliably predict response to immunotherapy. However, there are other tumour-related factors that might affect response, such as lymphocytic infiltrate, PD-L1 positivity, high interferon gamma signature and high tumour mutational burden.[100] It is likely that, with advances in genomic research, better predictors of response to both targeted and immune-mediated treatments will become available.

Dermatologist's role in patient advocacy and public health campaigns in skin cancer in Europe

Since the majority of skin cancers are attributable to UVR and, thus, potentially preventable,[11] a major role of dermatologists focuses on raising public awareness and leading public health campaigns. Although the real impact of sun protection and early detection on the long-term mortality of skin cancers is yet undetermined, Australian initiatives and successes are encouraging for European stakeholders to promote similar measures.[101,102] It is, therefore, crucial to strengthen bonds with key policy actors at national and international levels to bring this important health issue to the forefront of the health agenda.[103] Already since 2007, EADV together with Euromelanoma, the European Cancer Leagues and Members against Cancer started a dialogue and held press conferences in the EU Parliament, supported by the World Health Organization. Their objectives were to promote the importance of early diagnosis of skin cancer, discuss ways to improve skin cancer registration, emphasize the danger of using sunbeds and create awareness and protect the vulnerable group of outdoor workers exposed to occupational UVR. In outdoor workers, UVR is an inevitable carcinogen; therefore, the prevention and management of UVR-related skin cancers in these at-risk populations represent a collective challenge for dermatologists and healthcare policymakers likewise.[104] Since then, such activities have been held regularly in the EU parliament and have resulted in numerous questions addressed by Parliament members to the Commission to attract attention and obtain answers on these key issues. Furthermore, charts, call to actions and 'white books' have been drafted for these important issues, co-signed under EADV initiatives bringing together all important associations and stakeholders.

Meanwhile, with the Euromelanoma campaign that started in Belgium in 1999 and is now active in 33 countries, European dermatologists have succeeded in reaching the public, creating awareness of skin cancer and the importance of early detection by offering free annual skin cancer checks.[26] The high acceptance of this initiative shows the pivotal interest of the public in this issue at all ages. While skin cancer is the most common type of cancer in adults, it is considered rare in children. However, children are the most susceptible to UV damage and are a very important group to reach to promote primary prevention messages in order to reach their parents and avoid early-in-life damage exposure with life-long increase of oncogenic risk. As a

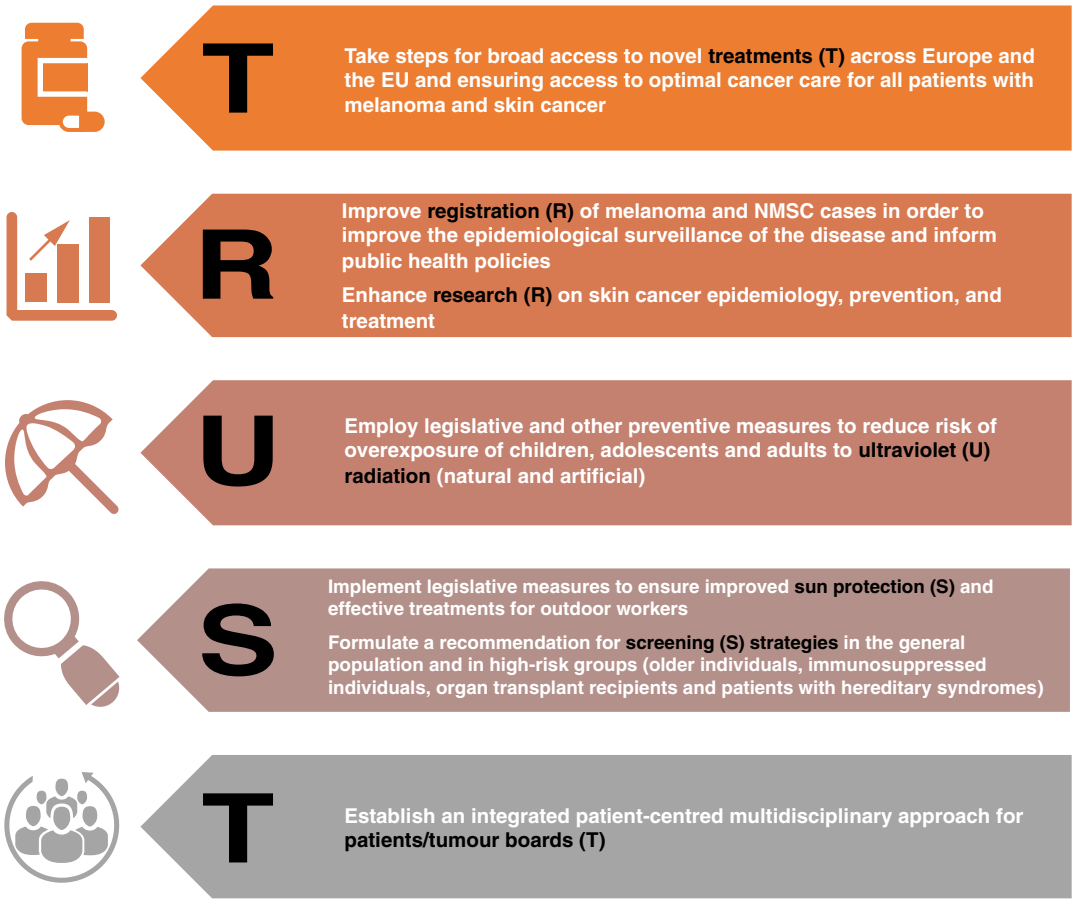

Figure 3 Addressing public health priorities in dermato-oncology (T.R.U.S.T.). HCPs: healthcare providers; NMSCs: non-melanoma skin cancers.

result, dermatologists in different European countries have led campaigns in schools to educate as early as possible on safe behaviour in the sun.[105,106]

Some of the most common situations that need careful input from dermatologists are solid organ or hematopoietic stem cell transplantation, cancer and cancer treatments, genodermatoses and hereditary cancer syndromes, patients with sensitive skin to sun damage, family history of skin cancer (especially melanoma), medications that suppress or modify the immune system, medications that induce photosensitivity and history of extensive sun exposure or use of tanning beds/indoor tanning.[101,102]

Finally, patient knowledge and fears about skin cancers as well as the burden associated with these lesions have not been clearly established. Dermatologists are among the most consulted medical specialists in Europe.[101,103,107] They are perceived by the general public as both fundamental caregivers for mole checking/melanoma screening and nevi removal, but awareness of their specific expertise in the diagnosis and treatment of all skin cancers is not optimal.[108–110] Furthermore, in many countries, GPs, or primary care physicians/providers (PCPs) are usually the first healthcare providers to be consulted for skin problems. Better training of GPs/PCPs in the detection of skin cancers in conjunction with better coordination of the patient care pathway from the GP/PCP towards the dermatologist is mandatory. In addition, heterogeneity in patient care pathways and healthcare systems across Europe must be articulated with a general public understanding that dermatologists are the specialists to be referred to when skin cancers are detected by other clinicians.

The EADV is currently launching a pan-European survey to better identify all potential barriers to overcome in order to reduce the delay between detection of a tumour and its management, in order to optimize care and devise efficient educational strategies that will help lead patients with skin cancer to the appropriately skilled specialist (i.e. the dermatologist).

Conclusions

The field of dermato-oncology is wide and evolving. As new insights emerge on the genetic and molecular mechanisms of cutaneous oncogenesis, transformative technologies are being incorporated into the diagnostic field, and novel treatments are being implemented in the management of advanced cutaneous tumours. These impressive changes have changed dermato-oncology dramatically from a narrow field with limited resources, to a rapidly expanding discipline with improved patient outcomes and a broader care perspective. This tremendous progress opens up new priorities and needs on a public health scale which are summarized in Fig. 3 (acronym 'TRUST'). Dermatology–Venereology has played a major part in these advances, ranging from prevention to multidisciplinary care, and from early diagnosis to more precise disease staging and structured comprehensive care. There is currently a need to broadly establish a dermato-oncology training curriculum and clinical care programmes which uniformly meet a high level of quality across Europe, in order to ensure that dermatologists continue to play a leading role in the evolving multidisciplinary patient-centred approach of patients with skin cancer.

Acknowledgements

We acknowledge the members of the Skin Cancer Unit and the Dermatology Department of the Hospital Clinic of Barcelona. We acknowledge the support by Maarten Vermeer, Antonio Cozzio, Rudolf Stadler, Pablo Ortiz-Romero, Julia Scarisbrick and Robert Knobler. Open access funding enabled and organized by Projekt DEAL.

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